EXHIBIT 16

OMB No. 0990-0115

Electronic Request for Proposal
SECTION A – SOLICITATION/CONTRACT FORM

OFFERORS ARE RESPONSIBLE FOR ROUTINELY CHECKING THE CMB WEBSITE http://www.niaid.nih.gov/contract/default.htm FOR ANY POSSIBLE SOLICITATION AMENDMENTS THAT MAY BE ISSUED. NO ADDITIONAL NOTIFICATION OF ANY AMENDMENTS WILL BE PROVIDED BY THIS OFFICE.

Purchase Authority: Public Law 92-218, as amended.
NOTE: The issuance of this solicitation does not commit the government to an award.

RFP Number:	*Just In Time:*		*Level of Effort:*
NIH-NIAID-DMID-04-49	[ ] Yes [X] No	Small Bus. Set-Aside [ ]Yes [X]No 8(a) Set-Aside [ ]Yes [X]No NAICS Code: none Size Standard: none	[ ] Yes [X] No *Total Effort:* [N/A]

TITLE: Production and Testing of a Modified Vaccinia Ankara (MVA) Vaccine

Issue Date: **December 4, 2003**	*Due Date:* **February 4, 2004** *Time:* **4:00 PM, EST**	*Technical Proposal Page Limits:* [ ] Yes *(see "How to Prepare and Submit Electronic Proposals")* [X] No

ISSUED BY:	[X] ***We reserve the right to make awards without discussion.***	
Jacqueline C. Holden Senior Contracting Officer Contract Management Program, DEA NIH, NIAID 6700-B Rockledge Drive Room 2230, MSC 7612 Bethesda, MD 20892-7612	***NO. OF AWARDS:*** [ ] Only 1 Award [X] Multiple Awards	***PERIOD OF PERFORMANCE:*** 3 years beginning on or about 07/30/2004

Offers will be valid for 120 days unless a different period is specified by the Offeror on the form entitled "Proposal Summary and Data Record, NIH-2043" (See SECTION J - Attachments)

The Official Point of Receipt for the purpose of determining timely delivery is the Contract Management Branch as stated above. The paper copy with original signatures is the official copy for recording timely receipt. If the paper copy of your proposal is not received by the Contracting Officer or Designee at the place and time specified, then it will be considered late and handled in accordance with HHSAR 352.215-70 entitled "Late Proposals and Revisions" located in this Solicitation. FACSIMILE SUBMISSION OF PROPOSALS IS NOT ACCEPTABLE.

POINT OF CONTACT -- **Brenda Brooks** ***--COLLECT CALLS WILL NOT BE ACCEPTED--***

Telephone: Direct 301-435-2765 *Main* **301-496-0612**	*Fax* **301-402-0972**	*E-Mail* **bbrooks@niaid.nih.gov**

Updated thru FAC 97-25 (05/02/01)

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INTRODUCTION AND BACKGROUND

Production and Testing of a Modified Vaccinia Ankara (MVA) Vaccine
RFP-NIH-NIAID-DMID-04-49

Introduction

The National Institute of Allergy and Infectious Diseases (NIAID) is the primary institute at the National Institutes of Health (NIH) for emerging infectious disease research, including research on pathogens that might be used as agents of bioterrorism. Bioterrorism is defined as the use of microorganisms, or the toxins released from them, that cause human disease or elicit widespread fear and intimidation of society.

The events of the past two years have significantly changed the world's perception of the nature and degree of the threats posed by the use of infectious agents as weapons of bioterrorism. The risk of using such weapons once appeared to be restricted to military encounters. However, the deliberate exposure of postal workers, other government employees and the American public at large to *Bacillus anthracis* spores highlighted the need to devise appropriate and effective measures to protect all U.S. citizens from the harmful effects of those biologic agents of most concern.

Background

Variola virus, the etiological agent of smallpox, is considered to have been one the greatest scourges on human health. The mortality rate of smallpox infection is approximately 30%, and individuals who recover from the infection frequently have disfiguring scars. It has been estimated that throughout recorded history more people died of smallpox than from all other infectious diseases combined. Fortunately, vaccination with a related, live, replicating, attenuated Orthopoxvirus (vaccinia virus) eventually led to the global eradication of this disease in 1979. Routine vaccination was halted shortly thereafter because the risks associated with vaccination outweighed the threat of the disease. Recent knowledge on the possible weaponization and availability of smallpox stocks to rogue nations has increased concern about the reemergence of this dreadful disease. As a result of this assessment, the U.S. Government is procuring enough replication-competent smallpox vaccine and bifurcated needles for every U.S. citizen.

Although the replicating smallpox vaccine (Dryvax®) presently employed to vaccinate U.S. military and first response personnel is highly efficacious, it is associated with significant local and/or systemic reactions in over 90% of vaccinees. Common mild side effects include redness and swelling at the site of vaccination, fever, and myalgia. Although rare in healthy individuals, more serious side effects include post-vaccinal encephalitis, eczema vaccinatum, disseminated vaccinia and death. The number of U.S. citizens at risk for these rare events has increased over the years due to: 1) life-saving drugs and medical procedures which compromise the immune system such as those drugs administered following organ transplant and, 2) the increased number of individuals infected with HIV. Concerns have also been raised over the possible association of vaccinia virus with angina, myo/pericarditis, ischemic heart disease and myocardial infarction. These facts have raised concerns about vaccinating every U.S. citizen with live, replicating vaccinia vaccine. Dryvax is presently contraindicated in individuals with a history of atopic dermatitis, eczema, heart disease, immunodeficiency, autoimmunity, or who are pregnant or lactating. It is also contraindicated to all who have close household contact with individuals who are immunocompromised, pregnant, or have a history of dermal disease. As of June 20, 2003, only 37,802 civilians, out of the 450,000 first-responders originally anticipated, had been vaccinated. The need for a safer smallpox vaccine is self-evident.

Modified vaccinia virus Ankara (MVA), a live, non-replicating form of vaccinia virus, was developed in Germany during the smallpox eradication period (1964-1970) as a "pre-vaccine" that was administered by intradermal injection followed by scarification with Lister-Elstree one to two weeks later. The goal of the combined vaccination was to induce immunity with MVA that would subsequently reduce the reaction to the replicating vaccine. While this dual vaccination strategy was tested in over 150,000 individuals (many of whom were at risk for vaccination with the replicating vaccine) with no adverse events, it was never tested for efficacy in preventing smallpox in endemic areas. MVA was derived from a more virulent form of a smallpox vaccine termed CVA by >500 serial passages in primary chick embryo fibroblasts (CEF). As a result of continuous passage *in vitro*, the viral genome suffered six major deletions and numerous mutations; of importance, MVA is missing at least two host range genes required for growth in mammalian cells, and several genes essential for viral immune evasion. MVA is incapable of amplification in human cells, and data suggest it can safely be administered to newborn mice, rabbits, chickens and immunosuppressed primates. MVA has been shown to protect nonhuman primates against challenge from monkeypox virus and variola virus, and more recently has been used safely as a gene delivery vector for HIV and cancer vaccines.

In February 2003, two contracts were awarded by NIAID as a result of RFP-NIH-NIAID-DMID-03-44. The main objectives of this solicitation were to: (a) produce 5,000 doses of MVA vaccine under manufacturing conditions that would enable the government to file an Investigational New Drug (IND) application for this product, (b) assess the immunogenicity and protection against lethal Orthopoxvirus challenge provided by MVA in small animal models, (c) develop a Clinical Plan for MVA and initiate a Phase I clinical trial, and (d) develop a feasibility plan to manufacture, formulate, fill, test and deliver up to 30 million doses of MVA vaccine for the U.S. Government.

Objectives

The primary purpose of this RFP (NIH-NIAID-DMID-004-49) is to continue advanced development and manufacture of an MVA vaccine. It is intended to target MVA vaccine candidates that can be produced at a scale to support commercial manufacturing, and that have demonstrated safety and immunogenicity in extensive preclinical studies. Although licensure of an MVA vaccine is not planned within the timeframe of this RFP, all activities and studies conducted in response to this RFP shall be those required for a licensure path.

This advanced vaccine research and development effort is milestone-driven and funding is expected to occur in phases. Periodic assessments of progress will be conducted by NIAID (*See Notes to Offerors #5 and #9*). Continuation of effort on initial and subsequent milestones and associated funding will be based on contractor performance, timeliness and quality of deliverables, and consultations between the contractor, NIAID staff, interagency working group members, and a Blue Ribbon Panel if one is appointed by NIAID.

Data provided in support of the proposed vaccine candidate will be based on a vaccine and manufacturing process that approximates the final product and process to be licensed. Either preclinical and/or clinical studies may be necessary to bridge between product manufactured at pilot lot and intermediate scales. Due to associated time and risk considerations, studies to bridge between products that are different, or that are produced by different manufacturing schemes, will not be acceptable unless adequate data are presented in the proposal to confirm that milestones and deliverables contained in this RFP can be met.

In addition, it is deemed critical that the offerors understand that the NIAID, on behalf of the U.S. Government, is committed to furthering the database on MVA vaccines in order to facilitate their use in protecting the public. This NIAID MVA vaccine development effort continues an advanced research and development program intended to generate data that will provide the U.S. Government with critical information regarding future procurement of MVA vaccine for the National Strategic Stockpile. Funding advanced development of more than one vaccine candidate should facilitate the process of gathering essential data. Developing multiple MVA vaccine candidates will also help insure a successful outcome by reducing the risk inherent in a contract effort based on a single vendor. Based on the fact that more than one candidate vaccine will be developed, it is the responsibility of the NIAID to compare their immunogenicity and efficacy. Accordingly, it should be expected that during the course of this contract the NIAID will directly fund, under another contract, animal immunogenicity and efficacy studies that will compare the candidate vaccines. The design of the essential animal challenge studies will be recommended and coordinated through the MVA Interagency Working Group, which includes representation from the NIH, Center for Biologics Evaluation and Research (CBER), United States Army Medical Research Institute of Infectious Diseases (USAMRIID) and Centers for Disease Control and Prevention (CDC). In addition to conducting its own animal studies, the NIAID is expecting to perform independent clinical studies that will compare the immunogenicity, reactogenicity, and preferred route of administration of candidate vaccines.

Participation in NIAID's initial RFP (NIH-NIAID-DMID-03-44) is not a pre-requisite for participation in this RFP.

Awards

It is anticipated that one or more completion type contract(s) will be awarded under this RFP. Each contract will manufacture, fill, finish, and release 3 million doses of MVA from at least three cGMP consistency lots within the first two years of award. The vaccine shall be of a quality suitable for a path to licensure in the U.S. The third year of the contract will allow for preclinical study and clinical trial follow-up, maintenance and storage of the vaccine inventory, stability testing, etc. As such, the budget for third year efforts will represent a small portion of the total budget proposed.

Dryvax® is a registered trademark of Wyeth.

STATEMENT OF WORK

Production and Testing of a Modified Vaccinia Ankara (MVA) Vaccine RFP-NIH-NIAID-DMID-04-49

Independently, and not as agent of the U.S. Government, the Contractor shall furnish all the necessary services, qualified personnel, material, equipment, and facilities not otherwise provided by the U.S. Government, as needed to perform the work described below.

See Notes #4 and #12 to Offerors.

Milestones: Consistent with the urgent requirements of this RFP, the Contractor shall submit and execute a plan to accomplish the following milestones. Unless otherwise agreed, all milestones will conclude with delivery of a final milestone report to the NIAID.

See Notes #1, #3, #6 and #7 to Offerors.

1. **Milestone 1 Product Development Plan:** Within 2 months of contract award submit a Product Development Plan (**PDP**) that is integrated with the quality, testing, and regulatory plans. Activities in this plan, for both the Active Pharmaceutical Ingredient (API) and final dosage form, shall focus on the following: (a) development, scale-up and validation of the manufacturing processes; (b) development optimization, and qualification/validation of the test methods necessary for product characterization, release testing, stability testing, and potency evaluation; and (c) stability studies for each formulation and container/closure. The PDP shall include all planned development activities including GMP as well as non-GMP studies. Timing of these activities relative to the manufacture of 3 million doses of MVA vaccine, as well as ultimate FDA licensure of the product (although not a requirement of this RFP), should be stated. Development, validation and stability programs must comply with current regulations and relevant FDA and ICG guidance documents.

   See Note #2 to Offerors.

   The NIAID is requesting that the API be at a concentration of 1×10^8 $TCID_{50}$ per dose, and the final dosage form be in a liquid formulation.

   See Notes #15 and #16 to Offerors.

2. **Milestone 2 Quality Systems Plan**: Within 3 months of contract award submit a Quality Systems Plan (**QSP**) that is integrated with the manufacturing, testing and regulatory plans. Activities in this plan shall focus on cGMP compliance for the production and release of both the Active Pharmaceutical Ingredient (API) and the 3 million doses of MVA. It shall include appropriate documentation of cells and/or cell banks used, change control, document control, environmental and utility monitoring, laboratory controls, maintenance and calibration, materials management (including shipping), Quality management, equipment qualification, computer validation, cleaning validation, production records (including deviations), laboratory records (including out of specifications results), and training. Quality systems must comply with current regulations and relevant FDA and ICH guidance documents.

3. **Milestone 3—Clinical Testing Plan**: Within 4 months of contract award submit a Clinical Testing Plan (**CTP**) to licensure that is integrated with the animal testing, manufacturing and regulatory plans using the most current and available information including consultation with DMID, CBER and other experts in the field. Clinical trial activities performed as a result of this solicitation shall include: (a) a dose-response trial in healthy adult populations (male and female) which are vaccinia naïve and previously vaccinated against smallpox, (b) a safety and immunogenicity trial with a fixed effective dose of MVA as determined in the dose-response trial, (c) a safety and immunogenicity trial in subjects with diagnosed atopic dermatitis, and (d) a safety and immunogenicity trial in subjects with HIV infection. At least one study shall include a healthy cohort(s) that may be followed for at least two years. Unless otherwise specified, all MVA vaccinations shall be administered via the subcutaneous route. Alternative routes of vaccine delivery will be studied by the DMID during the course of this contract. Although Phase III trials are not a requirement of this RFP, the CTP shall include future plans for these studies.

   It is recommended that the dose-response clinical trial be initiated as soon as possible. It is also expected that the Contractor shall provide the NIAID with all relevant information and/or the ability to cross-reference an IND in order to support NIAID filing a U.S. Government held IND. To facilitate rapid product development, the Contractor shall

provide NIAID with copies of all communications with FDA, and include NIAID staff in conference calls with the FDA. For information regarding the filing of an IND see http://www.fda.gov/cber/ind/ind.htm.

Standardized protocols, characterized reagents, and validated assays shall be used in all human trials. DMID will facilitate attaining necessary resources to ensure that immunological assays of samples obtained from all clinical trials are evaluated using standardized validated assays. The CTP shall include arrangements for delivery of clinical trial samples to the DMID and/or its designee(s).

4. **Milestone 4 Animal Testing Plan**: Within 5 months of contract award, submit an Animal Testing Plan (ATP) to vaccine licensure that is directed towards meeting the requirements of 21 CFR 601.91 (FDA Animal Rule) and that is integrated with the clinical testing, manufacturing and regulatory plans using the most current and available information derived from consultations with DMID, CBER, and other experts in the field. The ATP shall: a) be such that efforts and budget for all animal studies are "front-loaded" so that the maximum amount of data are acquired within the first two years of the contract; b) include a description of the animal experiments (supporting and pivotal) that will be conducted to study immunogenicity and efficacy, and ultimately support licensure under 21 CFR 601.91; and c) include a description of the assays (including a plan for validation) that will be used to study both humoral and cell-mediated immunity.

   The following is a list of points to consider in preparing the ATP: a) an appropriate animal model is chosen that will provide data of sufficient statistical significance or greater to support licensure under 21 CFR 601.91; b) a murine model is selected that demonstrates protection against a lethal aerosol challenge by ectromelia virus; c) a nonhuman primate model is utilized that is suitable for testing the efficacy of the vaccine to protect against challenge with monkeypox virus; and d) all pivotal studies leading towards licensure are conducted using Good Laboratory Practices (GLP). These points to consider are not meant to reflect official U.S. Government policy with regards to fulfillment of the requirements of 21 CFR 601.91; they are provided as a minimal framework for the ATP, and points for discussion with the CBER.

   In addition to the animal experiments proposed in fulfillment of 21 CFR 601.91, the ATP shall include separate section describing a formal toxicology study plan suitably tailored to measure the unique safety aspects of MVA. The Contractor shall initiate immunogenicity and toxicity studies only upon Project Officer approval.

5. **Milestone 5 Regulatory Support Plan**: Within 6 months of contract award submit a Regulatory Support Plan (RSP) that is integrated with all testing and manufacturing activities. Activities in this plan shall include Investigational New Drug (IND) maintenance, communications with the CBER, and the compilation of data and materials that will be required in the Biological License Application (BLA).

6. **Milestone 6 Summary Report**: Within 8 months of contract award, or sooner if available, provide a formal summary report to the DMID based on items described in the PDP and QSP. The report shall document the quality assurance procedures, performance measures, and quantitative performance targets associated with manufacture of 3 million doses of MVA vaccine. The Contractor shall demonstrate to the DMID that the final production facility is suitable for the manufacture of FDA-licensable MVA vaccine. The facility and production processes shall be maintained at current Good Manufacturing Practice (cGMP) standards throughout all manufacturing operations. Quality Control (QC) and Quality Assurance (QA) programs must be in place and sufficient to ensure cGMP manufacture of 3 million doses of MVA vaccine product. Quality programs must be maintained at cGMP standards throughout all manufacturing operations. Completion of this milestone is contingent upon a successful preproduction audit to be conducted by the DMID and/or its designee(s).

7. **Milestone 7:** Within 11 months of contract award, complete manufacture, test, fill, finish, release, store and/or deliver to the NIAID 500,000 single doses of MVA. The formulation, vial/closure of this vaccine shall be the same as that to be used to fulfill Milestone 13. The manufacture of this lot of vaccine shall be accomplished using the intermediate-scale technologies and procedures proposed in the Technical Section of the Proposal, and its intended purpose is to provide vaccine for both Contractor and NIAID sponsored clinical trials.

   See Note #14 to Offerors.

8. **Milestone 8:** Within 12 months of contract award, refine and submit for DMID approval, a plan to maintain, test and replenish the MVA vaccine inventory for the period of the contract. This milestone pertains to all activities required to maintain the vaccine inventory.

   See Note #13 to Offerors.

9. **Milestone 9 Large-Scale Production Plan:** Within 12 months of contract award, provide a Large-scale Production Plan (**LPP**) to manufacture, formulate, fill/finish, test, and deliver to the U.S. Government up to 50 million doses of the candidate MVA vaccine suitable for storage in a stockpile for emergency use. The purpose of the LPP is to demonstrate suitability to the U.S. Government as a supplier of MVA vaccine should the immediate need arise. The LPP shall be based on production of a stockpile produced from multiple, consistent, cGMP vaccine production campaigns, if needed. The plan shall include steps to be taken to monitor the quality of the vaccine product, and replenish the stockpile as needed to maintain its ready availability for emergency use under IND. The LPP shall include: a) details of the process to scale-up production of multiple lots, if needed b) a timeline for production and delivery of up to 50 million doses of product, c) a strategy that will be pursued to seek a U.S. license for the product and to provide continued support for maintaining an active government-held IND (this strategy shall be consistent with, and refined from, plans developed in the QSP and RSP and the Technical Proposal); d) estimates of cost/dose delivered in single-use vials; and e) a plan to monitor and replenish the stockpile as needed in consultation with managers of the U.S. Government stockpile (this plan shall be consistent with, and refined from Milestone 8).

10. **Milestone 10—Interim Clinical Trial Report:** Within 12 months of contract award or sooner if it becomes available, provide an Interim Clinical Trial Report that includes data summary and analysis, interpretation, and conclusions for the dose-response study. Also included in this report shall be a plan for refinement of follow-on clinical studies that may have been proposed in the CTP. The U.S. Government and/or the Contractor may use these data for consultations with the FDA concerning planning for subsequent product development.

    See Note #17 to Offerors.

11. **Milestone 11 Interim Animal Studies Report:** Within 16 months of contract award, provide an Interim Animal Studies Report derived from experiments proposed in the ATP. Included in this report shall be data summaries, analyses, interpretations, and conclusions of experiments conducted. Also included in this report shall be a plan for follow-on animal studies that may not have been proposed in the ATP. Lastly, in line with the requirement of 21 CFR 601.91 for GLP to be followed for pivotal studies, an interim qualification/validation report shall be prepared for selected animal models and their respective assays.

12. **Milestone 12:** Within 18 months of contract award, complete manufacture and release of bulk vaccine substance from at least three cGMP consistency lots. The bulk vaccine substance produced shall be sufficient for the fill/finish of 3 million single-doses.

13. **Milestone 13:** Within 21 months of contract award, complete formulation, fill and finish of all vaccine product that shall comprise the 3 million single-dose MVA vaccine inventory.

14. **Milestone 14:** Within 24 months of contract award, deliver and/or store for the U.S. Government, the entire 3 million dose inventory as directed. Lots may be delivered as they become available if approved by the Project Officer.

15. **Milestone 15:** Within 36 months of contract award, complete the **ATP** outlined in Milestone 4. Each GLP study shall be initiated following Project Officer approval of the plan and when suitable cGMP vaccine is available.

16. **Milestone 16:** Within 36 months of contract award, complete the **CTP and RSP** outlined in Milestones 3 and 5, respectively. The U.S. Government and/or the Contractor may use these data for consultations with the FDA concerning planning for subsequent product development.

17. **Milestone 17:** Within 36 months of contract award, complete the **PDP and QSP** outlined in Milestones 1 and 2, respectively.

18. **Milestone 18:** Within 36 months of contract award, store, maintain, test and replenish the vaccine inventory as needed. These activities shall begin after Milestone 7, when the first lot of vaccine is delivered to the DMID.

Meetings and Conferences: The Contractor shall participate in regular meetings to coordinate and oversee the contract effort as directed by the Project Officer. Such meetings may include, but are not limited to, meetings of all contractors and subcontractors to discuss preclinical and clinical study designs; meetings with individual contractors and other PHS officials to discuss the technical, regulatory and ethical aspects of the program; and meetings with NIH technical consultants to discuss data provided by the Contractor.

See Note #8 to Offerors.

[END OF STATEMENT OF WORK]

NOTES TO OFFERORS

Production and Testing of a Modified Vaccinia Ankara (MVA) Vaccine

RFP-NIH-NIAID-DMID-04-49

1. Offerors must submit a proposal in response to this RFP that has plans (Milestones 1, 2, 3, 4, 5, and 8) with sufficient detail to permit reviewers to make a realistic evaluation of the offerors likelihood of success. These milestones are included to allow successful offerors the ability to refine plans after award and after consultations with DMID and perhaps CBER. Technical detail in the proposal must be such that the preclinical, clinical, regulatory and stockpile maintenance plans requested for these milestones should require only minor changes after contract award. The cost proposal shall be broken out by Milestone. Budget detail for the clinical, regulatory and stockpile maintenance plans must be associated with, and reflect, the technical proposal.

2. It is expected that the API proposed for pilot-scale, intermediate-scale, and subsequently for large-scale manufacture, will be derived from the same Master Virus Seed (MVS) propagated in chick embryo cells. If a different MVS is used during the course of this contract, plans for animal studies and clinical trials should include control cohorts that monitor and compare the immunogenicity of different vaccine substances.

3. Plans associated with Milestones 1, 2, 3, 4, 5, and 8 must include a schedule for all activities through licensure. However, activities to be performed in response to this RFP, and consistent with the Period of Performance, must be clearly delineated. Budget shall be submitted only for activities proposed in response to this RFP that are consistent with the associated objectives, requirements, timelines and Period of Performance delineated in this RFP. Again, as much effort as possible with associated budget shall be performed in the first two years after contract award. The third year is primarily for follow-up to, and conclusion of, activities started in the first two years.

4. The Contractor shall develop and execute a Contractor's Work Plan (CWP) that describes the activities to be performed in response to the RFP requirements and a single Gantt chart that includes all activities described in the CWP with a time-phased and task-linked budget. The level of detail contained in the CWP and the corresponding Gantt chart will be sufficient to facilitate management and execution of the contract by the successful offeror. The primary milestones have potential to contain subcategories of secondary milestones such as cGMP manufacturing runs, individual animal studies and clinical trials. Minimally, cost proposals will be prepared based on the estimated cost of completion for each primary and secondary milestone.

5. The NIH reserves the right to conduct site visits when deemed necessary. These may include site visits to the contractor's or subcontractor's facilities during the proposal evaluation process and/or during contract performance. Such site visits may include other PHS officials or contractors representing NIH.

6. Cost proposals shall provide a breakdown of costs at the primary milestone and secondary milestone levels, minimally, as well as a cost estimate for the entire project.

7. The U.S. Government recognizes that some offerors may have already completed some of the tasks/milestones identified in the Statement of Work. In such instances, offerors' technical proposal must include sufficient information to support this claim and to allow for appropriate technical evaluation.

8. It is anticipated that a party of five from the Contractor shall participate in two-day visits every two months with the NIAID in Bethesda, MD.

9. The NIAID may convene an independent group composed of *ad hoc* experts and U.S. Government personnel that will provide DMID insight regarding manufacturing, testing and regulatory issues.

10. Any of the following plans and data available will be provided, if available, in the initial proposal or in the Final Proposal Revision (FPR):

    a. A Manufacturing Feasibility Plan for intermediate and large-scale manufacturing comprised of:
        - Facility status and availability
        - Manufacturing queue access/scale
        - Personnel availability and expertise
        - Performance history

- Estimated cost per dose (labor and materials broken out separately)
- Timelines
- Consistency of manufacture
- Licensure strategy
- Fill and storage capacity
- Stockpile maintenance plan

b. Mouse efficacy data or NHP efficacy data or both against challenge
c. IND submitted or cleared
d. Phase I and/or II safety and immunogenicity data
e. An animal testing plan to licensure
f. A clinical plan to licensure

11. Due to the urgent need to defend the American public against agents of bioterrorism, and the considerable investment by the U.S. Government in research and development required to procure the MVA emergency-use vaccine inventory that is the subject of this RFP, the U.S. Government expects and requires that the offeror will take all steps necessary to secure access to all intellectual property, know-how and tangible materials prior to contract award that the offeror needs to fulfill its obligation under the contract. Accordingly, the U.S. Government requires evidence at the time of proposal submission that the offeror has secured access to such intellectual property, know-how and tangible materials.

12. Funds will not be provided under the terms of this contract to develop the infrastructure required to implement large-scale manufacture.

13. Associated budget costs for additional lots produced to replenish the emergency-use inventory during the period of performance of this contract must be included in the proposal.

14. DMID requires that information required to conduct clinical trials under a U.S. Government-sponsored IND be submitted with the vaccine. Information required will include Pharmacology/Toxicology data, previous human data and authorization for the FDA to cross-reference either a Drug Master File or IND containing information relevant to chemistry, manufacturing and control data about the product.

15. It is presently expected that the maximum vaccine dose will be 10^8 $TCID_{50}$ MVA. If, in the course of this contract, the Contractor obtains clinical data that supports the effective use of a lower dose with their vaccine candidate, it may be possible to adjust the final vialing of vaccine product with the approval of DMID.

16. In light of the strict timeline requirements for characterization and production of MVA vaccine, it is suggested that it be delivered to the NIH and tested in preclinical and clinical studies in liquid formulation. However, it is recommended that associated budget costs be provided in the proposal for a concurrent small-scale investigation of a lyophilized vaccine product.

17. DMID requires that Interim Clinical Trial Reports be submitted for all studies planned under this contract. Since the start of the trials may be different for each contractor, individual Milestone requirements will not be set for the Interim Reports, but it is expected that they be submitted to DMID as soon as they become available.

REPORTING REQUIREMENTS

Production and Testing of a Modified Vaccinia Ankara (MVA) Vaccine
RFP-NIH-NIAID-DMID-04-49

The Contractor shall submit to the Contracting Officer and to the Project Officer technical progress reports covering the work accomplished during each reporting period. These reports are subject to the technical inspection and requests for clarification by the Project Officer. These shall be brief and factual and prepared in accordance with the following format:

A. Technical Reports

The Contractor shall prepare and submit the following reports in the manner stated below:

1. Monthly Technical Progress Reports—On the fifteenth of each month for the previous calendar month, the Contractor shall submit seven (7) copies of a Monthly Technical Progress Report, comprising six (6) copies to the Project Officer and one (1) copy to the Contracting Officer. Such reports shall include the following specific information:

   a. A cover page that lists the contract number and title, the period of performance being reported, the contractor's names and address, the author(s), and the date of submission;

   b. SECTION I—A listing of any and all deliverables submitted during the previous month, a listing of any and all relevant administrative items occurring in the previous months, a listing of all meetings held and meeting minutes submitted during the previous month, a brief summary of financial status of the Contract, and an introduction covering the purpose and scope of the contract effort;

   c. SECTION II—The report shall detail, document, and summarize the results of work done during the period covered and shall be organized by Milestones. These reports shall be in sufficient detail to explain comprehensively the results achieved. The description shall include pertinent data and/or graphs in sufficient detail to explain any significant results achieved and preliminary conclusions resulting from analysis and scientific evaluation of data accumulated to date under the project. Also to be included in the report is a summary of work proposed for the next reporting period. Specific requirements are set forth in the Work Statement. A one-page summary of each ongoing and completed protocol shall be submitted at this time. A monthly report will not be required for the period when the final report is due. Preprints and reprints of papers and abstracts shall be submitted with the Annual Report.

   d. SECTION III—Substantive performance; a description of current technical or substantive performance and any problems encountered and/or which may exist along with proposed corrective action. An explanation of any difference between planned progress and actual progress, why the differences have occurred, and if behind planned progress what corrective steps are planned. Also to be included in the report is a summary of any significant decisions taken/pending and concerns/strategies needing to be addressed.

2. Final Report—By the expiration date of the contract, the Contractor shall submit seven (7) copies of a comprehensive Final Report, as above, comprising six (6) copies to the Project Officer and one (1) copy to the Contracting Officer. This final report shall detail, document and summarize the results of the entire contract work for the period covered. This report shall be in sufficient detail to explain comprehensively the results achieved. Specific requirements are set forth in the Work Statement. Preprints and reprints not submitted previously shall be submitted.

3. Summary of Salient Results - With the annual/final reports the Contractor shall submit a summary (not to exceed 200 words) of salient results achieved during the performance of the contract.

B. Technical Report Distribution

Copies of the technical reports shall be submitted as follows:

Type of report	No. Copies	Addressee	Due Dates
Monthly Progress	6	Project Officer (P.O.) NIH/NIAID/DMID 6610 Rockledge Drive MSC 6605, Room 5121 Bethesda, MD 20892-7630	Specific dates will be listed in the contract document
Monthly Progress	1	Contracting Officer (C.O.) NIH/NIAID/CMB 6700-B Rockledge Drive MSC 7630, Room 2110 Bethesda, MD 20892-7610	Same as above
Milestone Reports	3	A milestone report will be provided after the completion of each Milestone unless otherwise agreed upon by the P.I. and the P.O.	Same as above
Final	7	Submitted with Final Report (six to Project Officer and one to Contracting Officer)	Expiration date
Summary of Salient Results	3	Same as above	Same as above

C. Deliverables

The following are considered deliverables under this contract:

1. All Technical Reports, Milestone Reports, preprints, and protocols as described in paragraph A, above. These deliverables are due as indicated.

2. All milestones indicated in the Statement of Work, including the following plans for specific milestones: Product Development Plan (Milestone 1); Quality Systems Plan (Milestone 2); Clinical Testing Plan (Milestone 3); Animal Testing Plan (Milestone 4); Regulatory Support Plan (Milestone 5); Summary Report (Milestone 6); Large-Scale Production Plan (Milestone 9); Interim Clinical Trial Report (Milestone 10); and Interim Animal Studies Report (Milestone 11).

D. General Requirements

Regular weekly meetings shall be held between the Principal Investigator and the Project Officer to monitor progress and address issues and concerns as may arise. These meetings will be held at NIAID offices or another mutually agreeable location or by telephone or videoconference at the discretion of the Project Officer. Other government or contract staff members or consultants may be asked to participate as appropriate. At least two (2) business days in advance of each weekly meeting, the Contractor shall provide to the Project Officer a written (E-mail) outline of the agenda for the upcoming weekly meeting. Within five (5) business days following each weekly meeting, the Contractor shall provide to the Project Officer a written (E-mail) summary of discussions at the last meeting, including documentation of any decisions made at the meeting.

PART I - THE SCHEDULE

SECTIONS B - H -- UNIFORM CONTRACT FORMAT - GENERAL

A Sample Uniform Contract Format may be found at the following website:

http://rcb.cancer.gov/rcb-internet/wkf/sample-contract.htm

PART II – CONTRACT CLAUSES

SECTION I - CONTRACT CLAUSES

THE FOLLOWING PAGES CONTAIN A LISTING(S) OF GENERAL CLAUSES WHICH WILL BE APPLICABLE TO MOST CONTRACTS RESULTING FROM THIS RFP. HOWEVER, THE ORGANIZATIONAL STRUCTURE OF THE SUCCESSFUL OFFEROR(S) WILL DETERMINE THE SPECIFIC GENERAL CLAUSES LISTING TO BE CONTAINED IN THE CONTRACT(S) AWARDED FROM THIS RFP.

ARTICLE I.1. GENERAL CLAUSES FOR A COST-REIMBURSEMENT RESEARCH AND DEVELOPMENT CONTRACT – FAR 52.252-2, CLAUSES INCORPORATED BY REFERENCE (FEBRUARY 1998)

This contract incorporates the following clauses by reference, with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available. Also, the full text of a clause may be accessed electronically at this URL: http://www.arnet.gov/far/.

a. FEDERAL ACQUISITION REGULATION (FAR) (48 CHAPTER 1) CLAUSES

FAR Clause No.	Date	Title
52.202-1	Dec 2001	Definitions
52.203-3	Apr 1984	Gratuities (Over $100,000)
52.203-5	Apr 1984	Covenant Against Contingent Fees (Over $100,000)
52.203-6	Jul 1995	Covenant Against Contingent Fees (Over $100,000)
52.203-7	Jul 1995	Anti-Kickback Procedures (Over $100,000)
52.203-8	Jan 1997	Cancellation, Rescission, and Recovery of Funds for Illegal or Improper Activity (Over $100,000)
52.203-10	Jan 1997	Price or Fee Adjustment for Illegal or Improper Activity (Over $100,000)
52.203-12	Jun 1997	Limitation on Payments to Influence Certain Federal Transactions (Over $100,000)
52.204-4	Aug 2000	Printing/Copying Double-Sided on Recycled Paper (Over $100,000)
52.209-6	Jul 1995	Protecting the Governments Interests When Subcontracting With Contractors Debarred, Suspended, or Proposed for Debarment (Over $25,000)
52.215-2	Jun 1999	Audit and Records - Negotiation (Over $100,000)
52.215-8	Oct 1997	Order of Precedence – Uniform Contract Format
52.215-10	Oct 1997	Price Reduction for Defective Cost or Pricing Data
52.215-12	Oct 1997	Subcontractor Cost or Pricing Data (Over $500,000)
52.215-14	Oct 1997	Integrity of Unit Prices (Over $100,000)
52.215-15	Dec 1998	Pension Adjustments and Asset Reversions
52.215-18	Oct 1997	Reversion or Adjustment of Plans for Post-Retirement Benefits (PRB) Other Than Pensions
52.215-19	Oct 1997	Notification of Ownership Changes
52.215-21	Oct 1997	Requirements for Cost or Pricing Data or Information Other Than Cost or Pricing Data - Modifications
52.216-7	Dec 2002	Allowable Cost and Payment
52.216-8	Mar 1997	Fixed Fee
52.219-8	Oct 2000	Utilization of Small Business Concerns (Over $100,000)

52.219-9	Jan 2002	Small Business Subcontracting Plan (Over $500,000)
52.219-16	Jan 1999	Liquidated Damages - Subcontracting Plan (Over $500,000)
52.222-2	Jul 1990	Payment for Overtime Premium (Over $100,000) (NOTE: The dollar amount in paragraph (a) of this clause is $0 unless otherwise specified in the contract.)
52.222-3	Aug 1996	Convict Labor
52.222-26	Apr 2002	Equal Opportunity
52.222-35	Dec 2001	Equal Opportunity for Special Disabled Veterans, Veterans of the Vietnam Era, and Other Eligible Veterans
52.222-36	Jun 1998	Affirmative Action for Workers with Disabilities
52.222-37	Dec 2001	Employment Reports on Special Disabled Veterans, Veterans of the Vietnam Era, and Other Eligible Veterans
52.223-6	May 2001	Drug-Free Workplace
52.223-14	Oct 2000	Toxic Chemical Release Reporting
52.225-1	May 2002	Buy American Act - Supplies
52.225-13	Jul 2000	Restrictions on Certain Foreign Purchases
52.227-1	Jul 1995	Authorization and Consent, Alternate I (Apr 1984)
52.227-2	Aug 1996	Notice and Assistance Regarding Patent and Copyright Infringement (Over $100,000)
52.227-11	Jun 1997	Patent Rights - Retention by the Contractor (Short Form) (NOTE: In accordance with FAR 27.303 (a) (2), paragraph (f) is modified to include the requirements in FAR 27.303 (a) (2) (i) through (iv). The frequency of reporting in (i) is annual.
52.227-14	Jun 1987	Rights in Data – General
52-232-9	Apr 1984	Limitation on Withholding of Payments
52.232-17	Jun 1996	Interest (Over $100,000)
52.232-20	Apr 1984	Limitation of Cost
52.232-23	Jan 1986	Assignment of Claims
52.232-25	Feb 2002	Prompt Payment
52.232-25	Feb 2002	Prompt Payment, Alternate I (Feb 2002)
52.232-34	May 1999	Payment by Electronic Funds Transfer--Other Than Central Contractor Registration
52.233-1	July 2002	Disputes
52.233-3	Aug 1996	Protest After Award
52.242-1	Apr 1984	Notice of Intent to Disallow Costs
52.242-3	May 2001	Penalties for Unallowable Costs (Over $500,000)
52.242-4	Jan 1997	Certification of Final Indirect Costs

52.242-13	Jul 1995	Bankruptcy (Over $100,000)
52.243-2	Aug 1987	Changes - Cost Reimbursement, Alternate V (Apr 1984)
52.244-2	Aug 1998	Subcontracts, Alternate II (Aug 1998) *If written consent to subcontract is required, the identified subcontracts are listed in ARTICLE B., Advance Understandings.
52.244-5	Dec 1996	Competition in Subcontracting (Over $100,000)
52.245-5	Jan 1986	Government Property (Cost-Reimbursement, Time and Material, or Labor Hour Contract)
52.246-23	Feb 1997	Limitation of Liability (Over $100,000)
52.249-6	Sep 1996	Termination (Cost-Reimbursement)
52.249-14	Apr 1984	Excusable Delays

b. DEPARTMENT OF HEALTH AND HUMAN SERVICES ACQUISITION REGULATION (HHSAR) (48 CFR CHAPTER 3) CLAUSES

HHSAR Clause No.	Date	Title
352.202-1	Jan 2001	Definitions - with Alternate paragraph (h) (Jan 2001)
352.228-7	Dec 1991	Insurance - Liability to Third Persons
352.232-9	Apr 1984	Withholding of Contract Payments
352.233-70	Apr 1984	Litigation and Claims
352.242-71	Apr 1984	Final Decisions on Audit Findings
352.270-5	Apr 1984	Key Personnel
352.270-6	Jul 1991	Publication and Publicity

END OF GENERAL CLAUSES FOR A COST-REIMBURSEMENT RESEARCH AND DEVELOPMENT CONTRACT – Rev. 4/2003]